Production of High Specific Activity ^{72}As, ^{77}As and ^{67}Cu for Research and Clinical Applications: *Effective design and recycling of targets and radioisotope separation.*

Collaboration with Silvia Jurrison, Cathy Cutler and team at University of Missouri

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Medical Isotope Research and Production Program

High Specific Activity ^{67}Cu and ^{72}As (BNL and MU)

Copper-67 has a 61.83 hours half life and is ideal for SPECT (Single Photon Emission Computer Tomography) and radiotherapy.

Arsenic (As) has several radioisotopes and so offers several options for applications medicine, toxicological and environmental studies.

Arsenic-72 (half-life 26 h) is the positron emitting daughter isotope of ^{72}Se (8.5 d) and provided for the option for a generator style production of ^{72}As.

Aim: Four Projects

***Project 1*: Production of high specific activity ^{67}Cu moderate energy protons (≈ 43 MeV):**

To produce high specific activity ^{67}Cu and minimize contamination by ^{64}Cu.

***Project 2*: Accelerator production of ^{72}As using protons of moderate energy (~50 MeV):**

(a) *To design a ^{nat}As target that **is robust at high proton currents** and capitalize on the high cross sections of the ^{72}As (p, 4n) ^{72}Se reaction; and*

(b) *To evaluate the radiation stability of an anion exchange ^{72}Se/^{72}As generator system containing up to 50 mCi of ^{72}Se recently developed (under DOE DE-SC000385 by Jurrison et al)*

Project 1 and 2 to be conducted at BNL
Transfer of 50mCi batches to Uni Missouri for generator work

Aims: Four Projects cont'd

***Project 3*: Reactor production of high specific activity ^{77}As:**

To make available a therapeutic radionuclide as a matched pair for the diagnostic ^{72}As.

***Project 4*: Development of a no carrier added (NCA) radioarsenic ($^{72/77}As$) precursor:**

To translate the radioarsenic chemistry developed during the previous DOE funding (DE-SC0003851) using carrier added ^{76}As to the NCA level.

Project 1 and 2 to be conducted at BNL
BNL to transfer of 50mCi batch of Se-72 to Uni Missouri for generator work

FWP Milestone Schedule for Project 1 and 2

Milestone	Timeline	Progress to date
Theoretical calc, Cu and Se procurement of equipment and **safety approval**	Y1 - Q2	80% Completed
Recruit post doctorate fellow	Y1 - Q2	Departed; Need to recruit again
Commence test irradiations Cu targets.	Y1 – Q2 - Q3	Commenced Jul 14
Complete validation of Cu-67 separation.	Y2 – Q4	Commenced Jun 15
Commence test irradiation of As targets.	Y2 - Q2	Commence Jul 2014
Validate As targets separation.	Y2 - Q3	To start in Y15

Project status

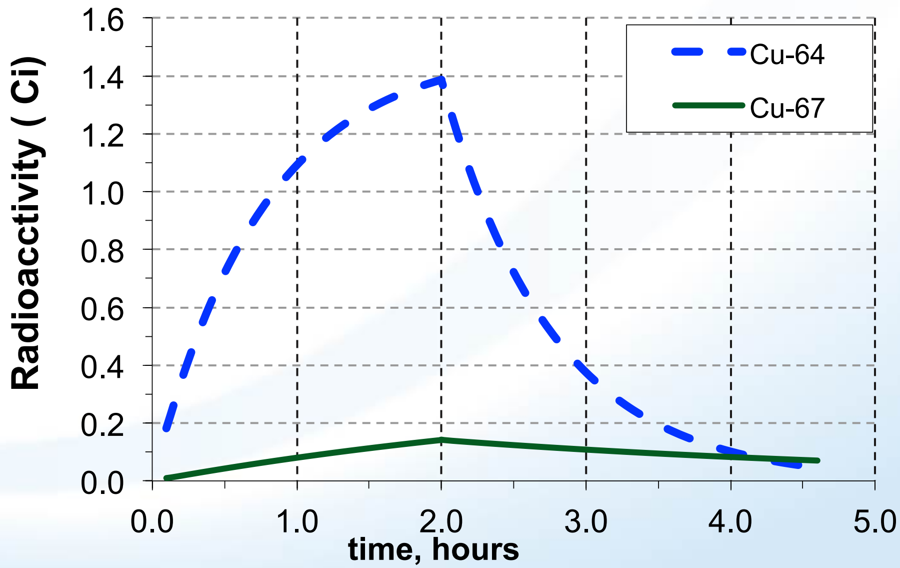
- Project commenced in July 2013 and due to complete July 2015 (2 years).
- Commitments of PI Smith to MIRP Production Program, as QA manager and Production Manager, redirected efforts.
- Major issues resolved in production; PI should be able to devote sufficient time in FY15.
- Request for an extension will be forwarded to DOE Isotope Program by end Dec 2014.

WBS or ID #	Item/Activity	Baseline Total Cost (AY$)	Costed & Committed (AY$)	Estimate To Complete (AY$)	Estimated Total Cost (AY$)
	^{72}As, ^{77}As and ^{67}Cu R&D	$ 750,000	$ 144,296	$ 605,704	$ 750,000
Totals:		$ 750,000	$ 144,296	$ 605,704	$ 750,000

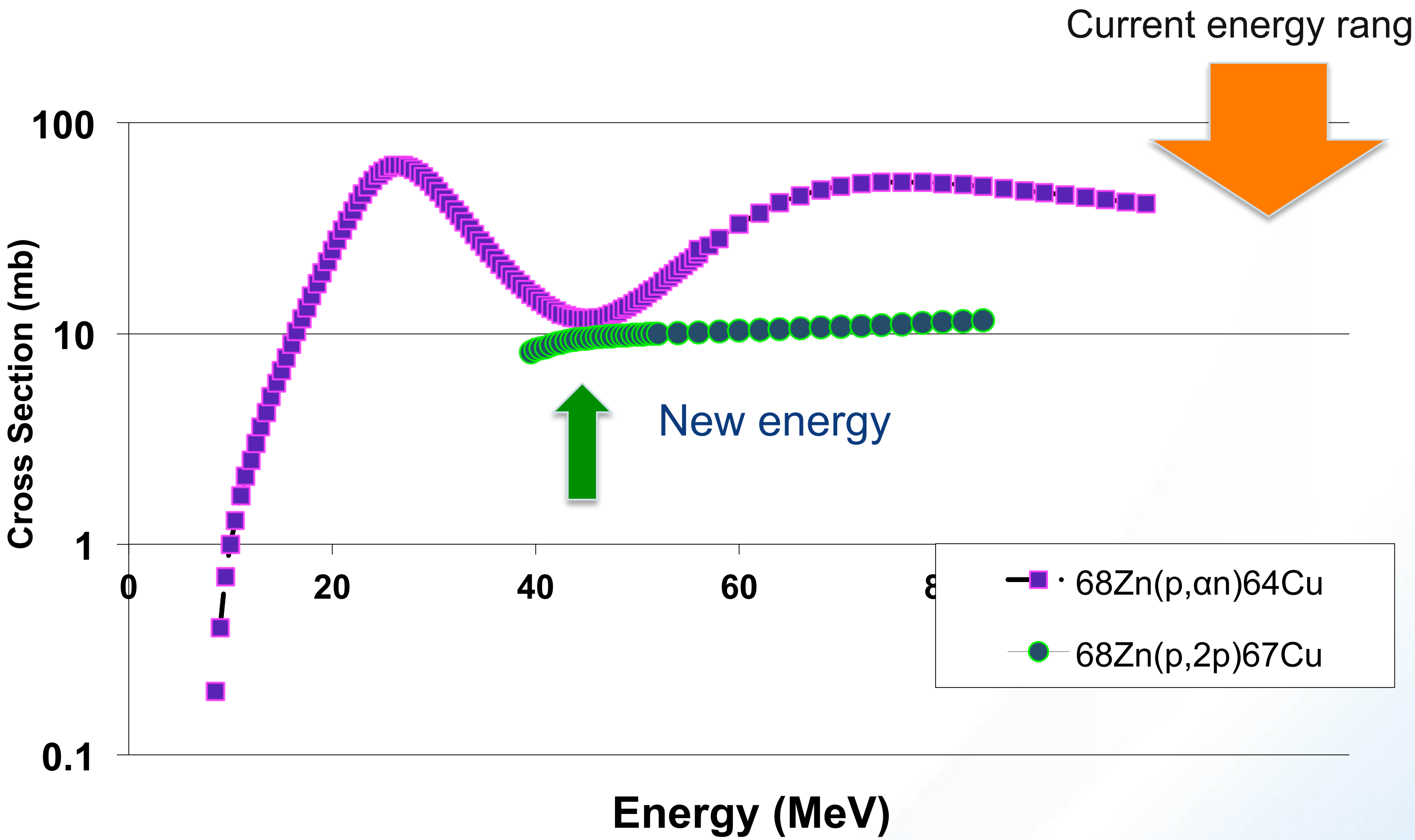
Project 1 – *Science*

High specific activity ^{67}Cu moderate energy protons (≈ 43 MeV)

- The ^{67}Cu is produced at BLIP using 100 -128 MeV protons.
- Typically 2 day irradiation of an enriched ^{68}Zn targets at 100 MeV produces ≈ 90-100 mCi of ^{67}Cu and 1400 mCi of ^{64}Cu.
- The mixture requires ^{64}Cu to decay for > 2 days before the ^{67}Cu activity exceeds that of ^{64}Cu.



Excitation Function for Production of ^{67}Cu using protons



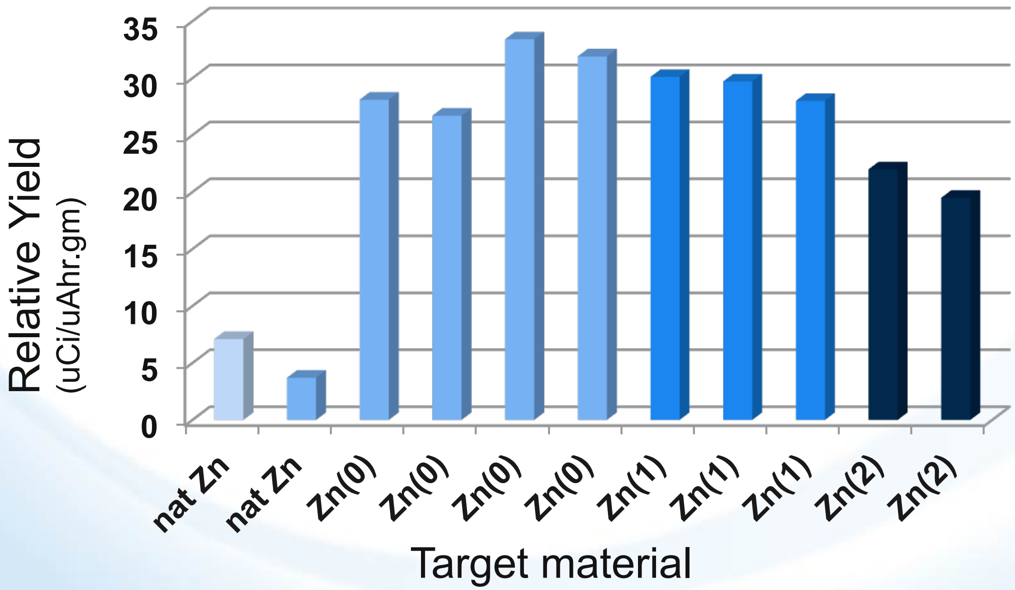
- Cross section data of 40 – 50 MeV protons on ^{68}Zn show a dramatic decline in ^{64}Cu production and a slight decrease in ^{67}Cu.
- Opportunity for new target array - shift Sr-82 to higher energies and position ^{68}Zn target in "low energy slot"

Current Process - Challenges

Current ^{67}Cu separation process based on 20 yr history, requires **three columns** and **a full day effort**.

- Column 1. removes $^{66/67}Ga$ from the $^{68}Zn/^{65}Zn$ target, $^{64/67}Cu$ and other contaminating radioisotopes [$^{56,57,58,60}Co$, ^{54}Mn]
- Column 2. separates $^{64/67}Cu$ from Zn target;
- Column 3. separates $^{64/67}Cu$ from remaining Co radionuclides.

Yields have varied from 16 to 31 µCi/µAh.gm of ^{68}Zn.



Relative yields decline depending on recycle times.

Note: Zn-68 targets Zn(0) untreated; Zn(I) recycled once, Zn(2) recycled twice.

Medvedev and Mausner Appl. Radiat. Isotope (2012)

This project progress to date

Evaluating three methods for separation of Cu radioisotopes from Zinc target. Method:

1) *Electroplating methods*
2) *Commercial Cu-resin*
3) *Cation and anion exchange resin using organic acid mixtures*

Method (1) Missouri Uni Post Doc Don Wycoff and BNL Post Doc Ramesh Sharma (1 week May 2014)
Method (2) PhD student - Anthony DeGraffenreid (3 week Sept and Aug 2014)
Method (3) Kylen Solvik (2013 Summer Intern) and Lisa Muench (1 wk Sept 2014)

High concentrations of Ga radioisotopes requires first

- *Separation of Ga from rest of digest or*
- *Cu from Ga to reduce dose to operator.*

Method (1)

Electrolysis - Isolation of copper from a zinc chloride solution

Electrolysis apparatus:	**Jurrison UM**
H-cell with **no applied potential** zinc anode and platinum cathode **one hour** electrolysis	Anode and cathode ionic strength are matched to minimize zinc ion migration across the sintered glass cell bridge
Cathode solution (platinum wire) ○ 25 mL ○ 0.12 M HCl ○ 1.23 M $ZnCl_2$ (2.0 g)	**Anode solution (zinc wire)** ○ 25 mL ○ 0.12 M HCl ○ 3.67 M NaCl
Using typical target size ○ Copper deposition follows **first order kinetics** ○ Platinum electrode **surface area is rate limiting** ○ With a 52 mesh Pt electrode, 2 cm x 5 cm, greater than 90 % of copper is deposited in 1 hour	
Copper removed from platinum electrode by acid or apply reverse potential	
	1. rinsing with dilute HNO_3 or 2. reverse electrolysis at 2.1 V
Reference: S. Mirzadeh, F. F. Knapp, Jr., Radiochim Acta, 57, 193-199 (1992)	

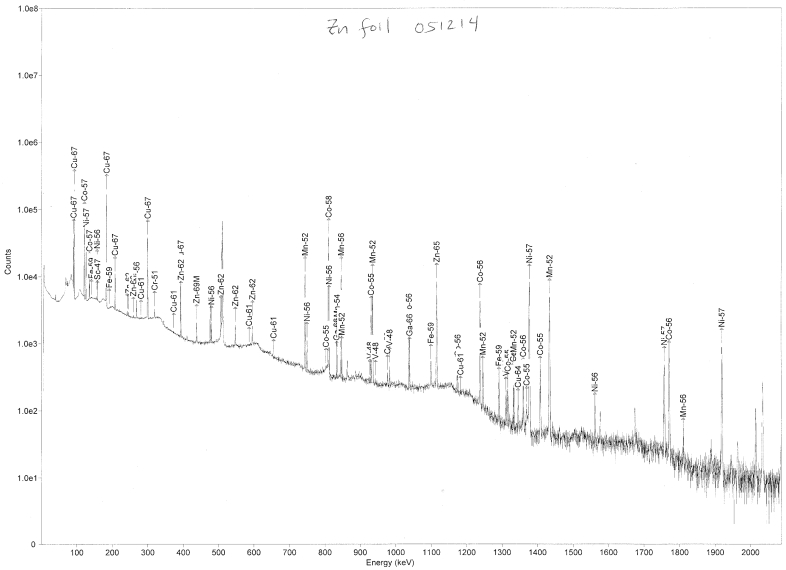


Fig 1. Gamma Spectrum of crude irradiated Zinc digest

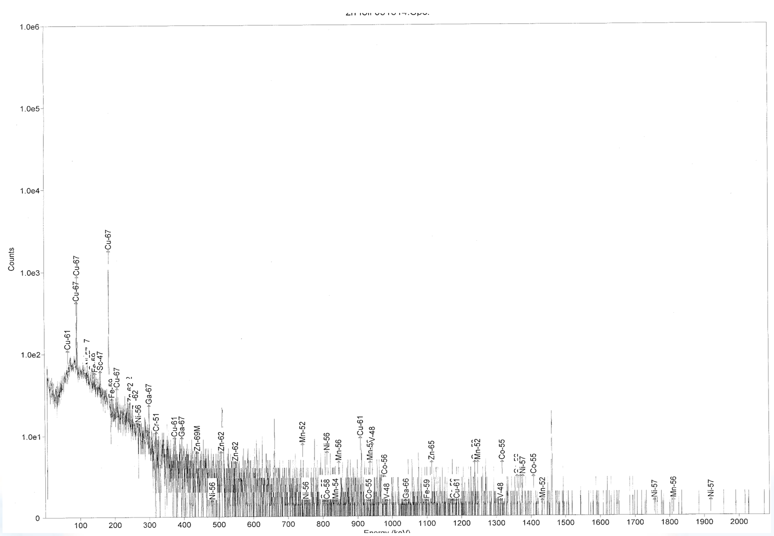


Fig 2. Gamma Spectrum of electroplated Cu radioisotopes from crude irradiated Zinc digest

Zinc foils irradiated at BLIP were digested and the resultant solution exposed to electrochemical cell using an platinum wire.

Fig. 1 shows the mixture of radionuclides present.

Fig. 2 shows the selected electroplating of Cu isotopes.

A new platinum cathode Fig. 3 with greater surface area is under construction for use.

The electroplating method will be tested in Feb 15 with irradiated foils

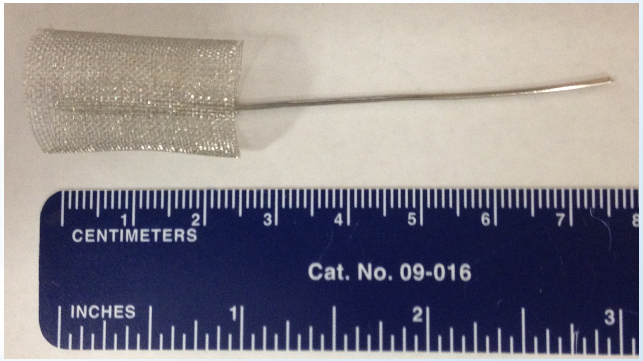
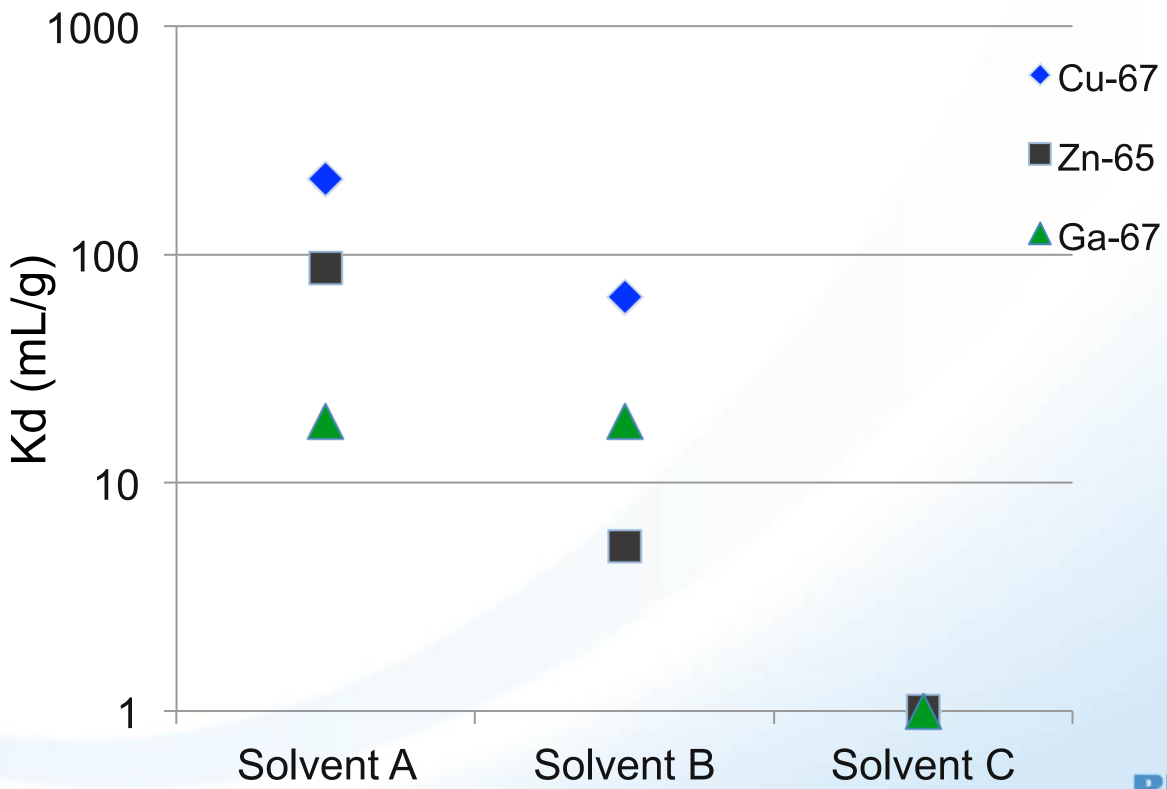


Fig.3. New Platinum electrode with large surface area.

Method (2)

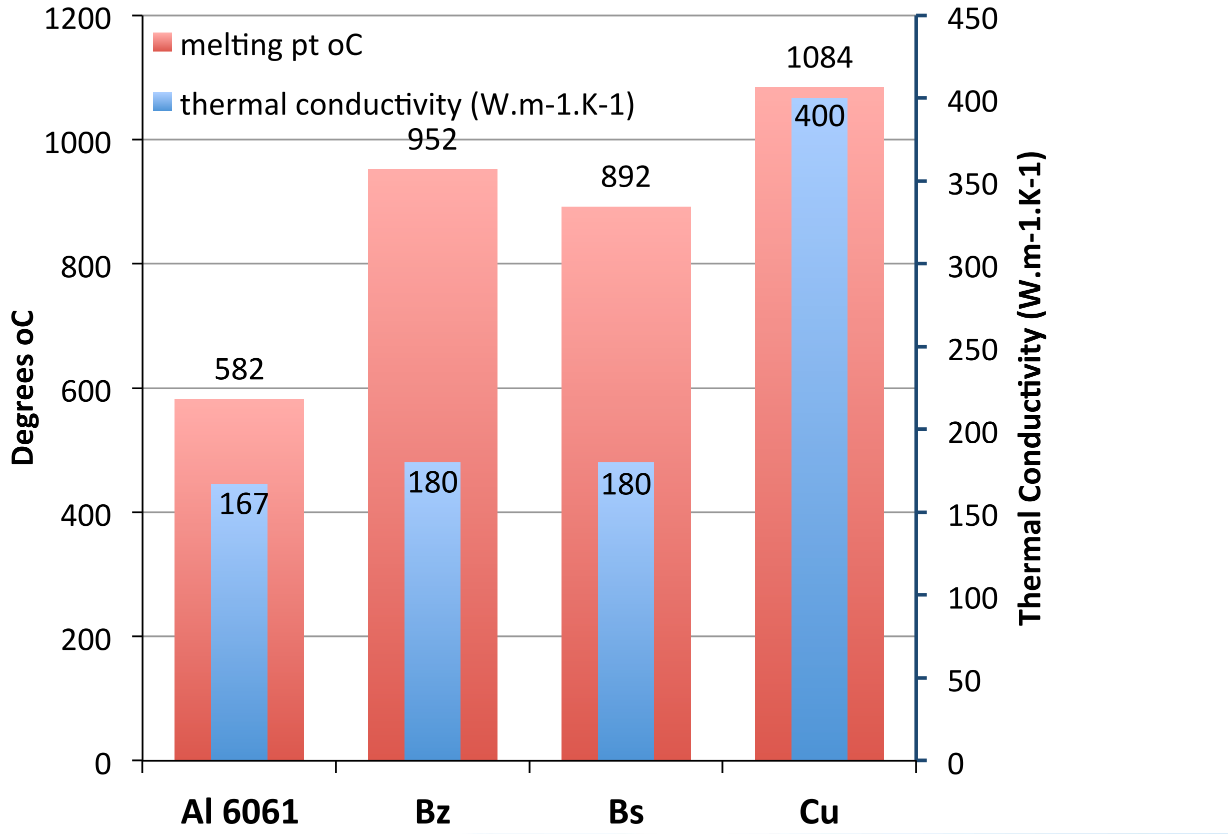
Cation and anion exchange resin using organic acid mixtures

Initial work on distribution coefficients for metal (Co, Zn, Ga, Cu, Mn, Fe) binding to cation exchange resin show separation of Ga and Cu is possible using organic acid mixture.

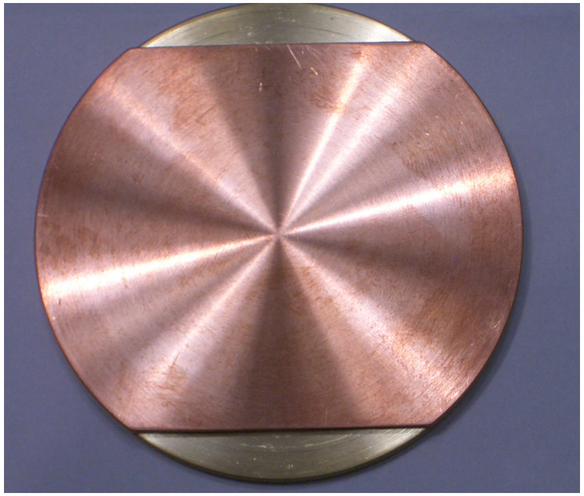


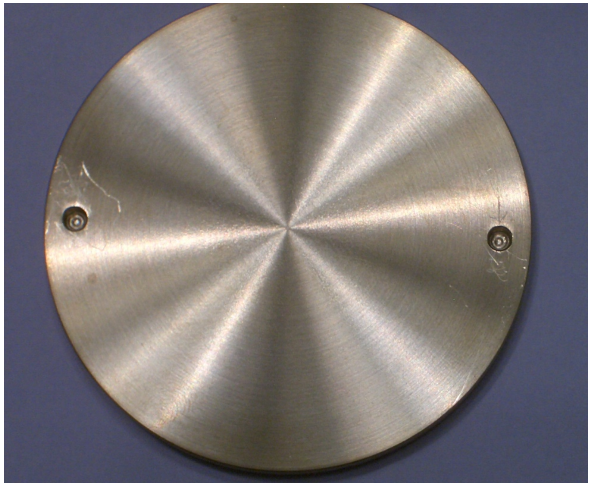
New target can constructed for Zn target irradiations.

Melting points and thermal conductivity of target can material.



Successfully passed initial irradiation test in BLIP in Jul 2013.

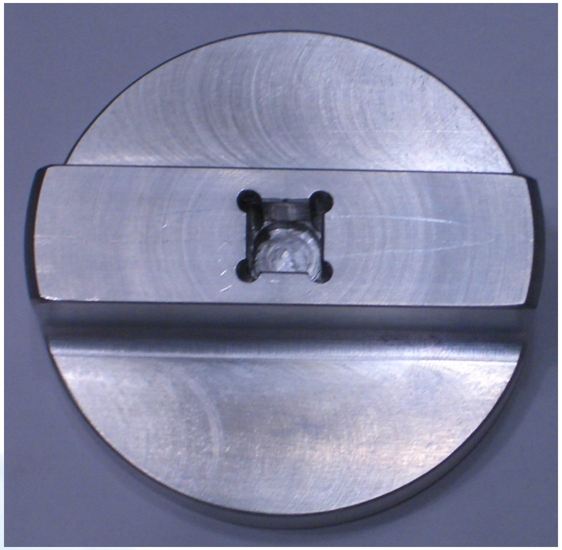


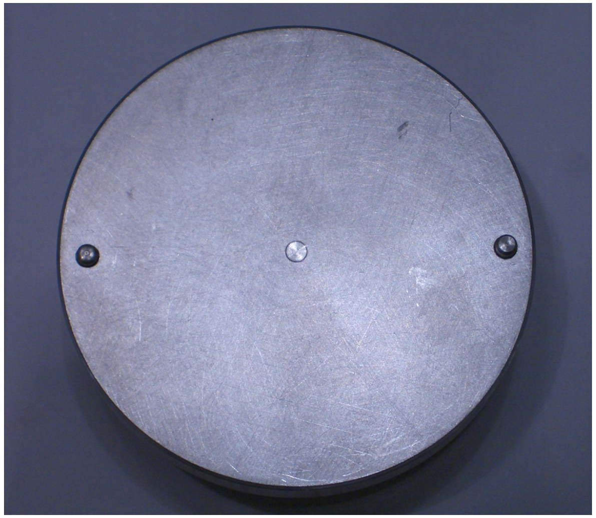


New target cans for zinc plating.

Nickel coating will protect Zn from Cu contamination.

Electroplating of target will commence in Mar 15





New target can opener designed for ready for testing in cell.

Project 2

Accelerator production of ^{72}As using ~50 MeV protons

- Proton irradiation of natural As is preferred for production of ^{72}Se and the literature.
- Alloys of As with copper (i.e. Cu_3As) have been produced in an effort to stabilize arsenic from volatilization during irradiation.
- Key performance criteria - production of ^{72}Se that is easily modified or adapted for incorporation of chemical separation methods established at MU.

Table 2. Compounds of As considered for the target material.

Material	Melting point	Comments
As metal	817^0 C at 28 atm	613^0 C subl, soluble HNO_3
As_2O_3	Decomposes at 312.3^0 C	water soluble
As_2O_5	315 ^{0}C	water soluble
As_2S_2	307 ^{0}C	water insoluble

Alloys of As and Copper (i.e. Cu_3As) have been produced in an effort to stabilize arsenic from volatilization during irradiation.

Final choice will depend on

- *The heat load calculations and*
- *Ease of chemical conversion to the desired ^{72}Se form*

Project 2

Preferred Se target material identified.

- In July we successfully tested a **new target material** at 50 MeV in BLIP for the production of Se-72.
- The **new target** was digested and initial studies show chemical separation of a number of radionuclides (Ge-68 and Se-72) are possible.
- **Patent protection** will be sort for this technology.
- New target material can be housed in new target cans.
- Supported the application of Matt Gott (PhD student U Miss) for a DOE Office of Science Graduate Student Research Grant Program to come for 4 months to BNL.